# Ionic-Liquid-Supported Synthesis of Amines and Derivatives

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**Abstract:** Amine precursors such as NH-Boc (**5**) and NH-formyl (**6**) protected glycines were grafted by esterification on the hydroxylated arms of 1-(2-hydroxyethyl)-3-methylimidazolium hexafluorophosphates **4*h*** or tetrafluoroborates **4*t***. The Boc cleavage was then realized at room temperature by successively treating acetonitrile solutions of the carbamates **7*h*** or **7*t*** with methanol and acetyl chloride (2 equivalents each). Interestingly, the hydrochlorides were converted to the corresponding amines **9*h*** or **9*t***, respectively, during the removal of the solvent. Ugi reaction of the ionic liquid-grafted amine **9b*t*** with phthalaldehydic acid and *tert*-butylisonitrile, followed by cleavage, furnished the phthalimidine **12**.

**Key words:** ionic liquids, amines, glycine derivatives, esters, Ugi reaction

## Introduction

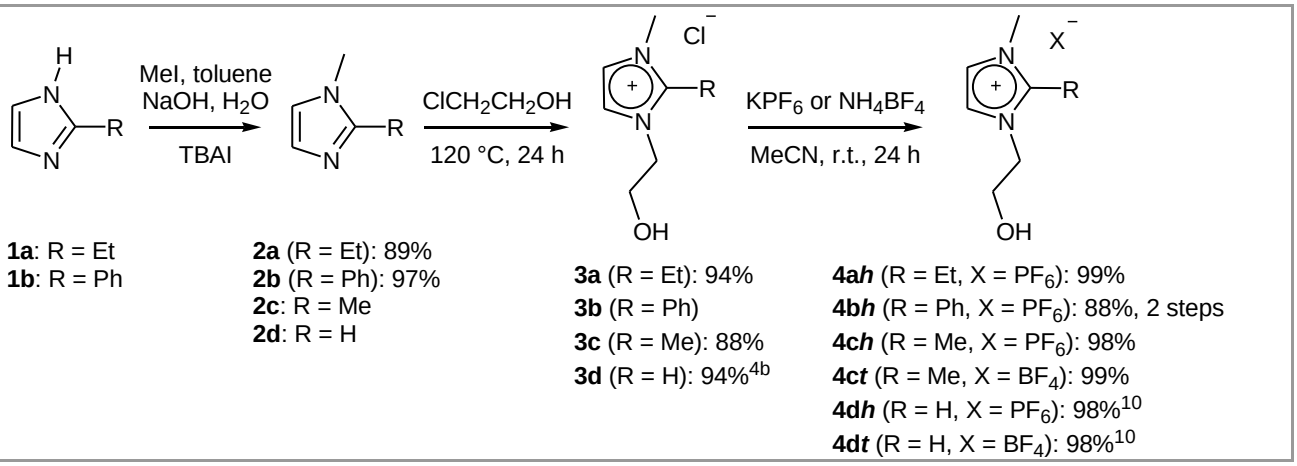
The demand for increasing numbers of compounds, notably with potential therapeutic value, caused chemists to look for ways to simplify, expedite, and automate the process of organic molecules syntheses. Since Merrifield introduced the solid-phase peptide synthesis,[1] insoluble supports rapidly developed into a means for facile purification processes, with easier phase separation and purification to remove excess reagents and side products, and possible automation. More recently alternative methodologies appeared in order to compensate for the drawbacks related to the heterogeneous nature of the insoluble polymers. Soluble polymer supports were aimed at restoring homogeneous reaction conditions although retaining the easy purification of the product;[2] however, limitations such as a low loading capacity can restrict their applications. The use of fluorous phase synthesis proved efficient for the separation of small molecules,[3] but the expense of perfluoroalkane solvents limits its development. In 2001, low molecular weight ionic liquids were used as soluble supports for organic synthesis.[4]

Ionic liquids, notably those including 1-alkyl-3-methylimidazolium cations, have been largely used in organic synthesis as reaction media.[5] A feature of ionic liquids is that their solubilities in organic and aqueous phases can be tuned by varying the nature of the anion and ring substituents. Taking advantage of this opportunity, labs including ours studied and demonstrated the efficiency of ionic liquid supported syntheses.[4,6] As a continuation of our work on functionalized ionic liquids, we have synthesized a series of amines that could be involved in multicomponent reactions utilizing isonitriles.

Few syntheses of amino ionic liquids are described in the literature.[6e,7] The amines we here describe are connected to the imidazolium parts with an ester function that could be cleaved to recycle the ionic support. Moreover, the substitution at C2 of the azolium ring was also considered for possible use in reactions with bases.[8]

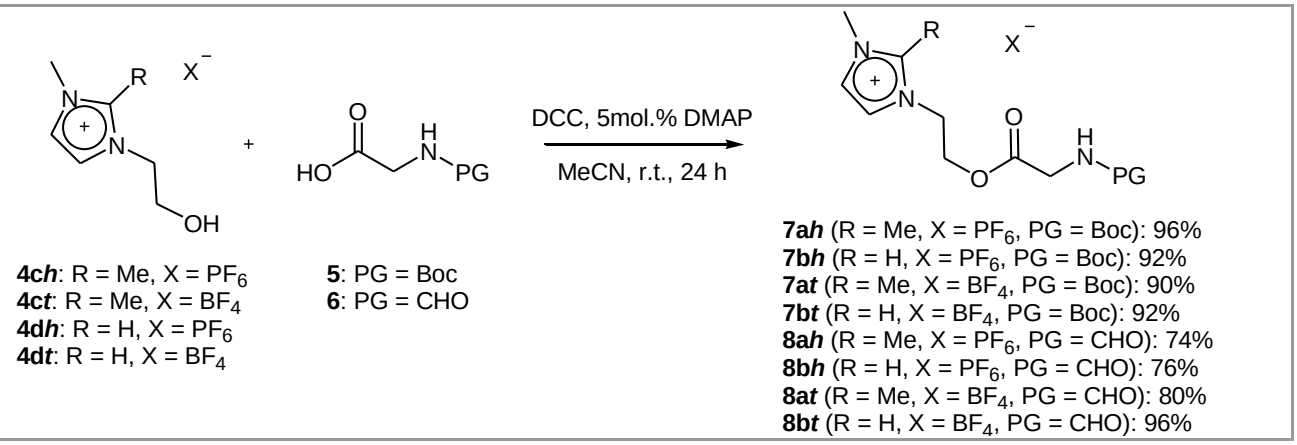
## Results and discussion

The synthesis of the 2-substituted 1-methylimidazoles **2a** and **b** from commercially available 2-ethylimidazole (**1a**) and 2-phenylimidazole (**1b**), respectively, was effected by improving a method described in the literature.[9] The use of iodomethane (2 equiv) in basic media under phase transfer catalysis afforded the expected methylated compound **2a** in 36% yield, due to the competitive formation of 2-ethyl-1,3-dimethylimidazolium iodide. Using a stoichiometric amount of iodomethane avoided the side-product to be formed, and afforded **2a** in 89% yield. The compound **2b** was similarly obtained in 97% yield. Quaternarisation of the 2-substituted imidazoles **2a-c** was carried out as described for the compound **2d**,[10] by simply heating the substrate with 2-chloroethanol at 120 °C. Except for the compound **3b**, which proved to be too viscous and was directly involved in the next step, the chlorides **3** were easily purified by washing with diethyl ether and drying. Anion metathesis using either potassium hexafluorophosphate or ammonium tetrafluoroborate was effected as reported for the compound **3d**.[10] Filtration of ammonium or potassium chloride, which are insoluble in acetonitrile, afforded the hexafluorophosphates **4a*h***, **4b*h***, **4c*h*** and **4d*h***, and the tetrafluoroborates **4c*t*** and **4d*t*** in excellent yields (Scheme 1).



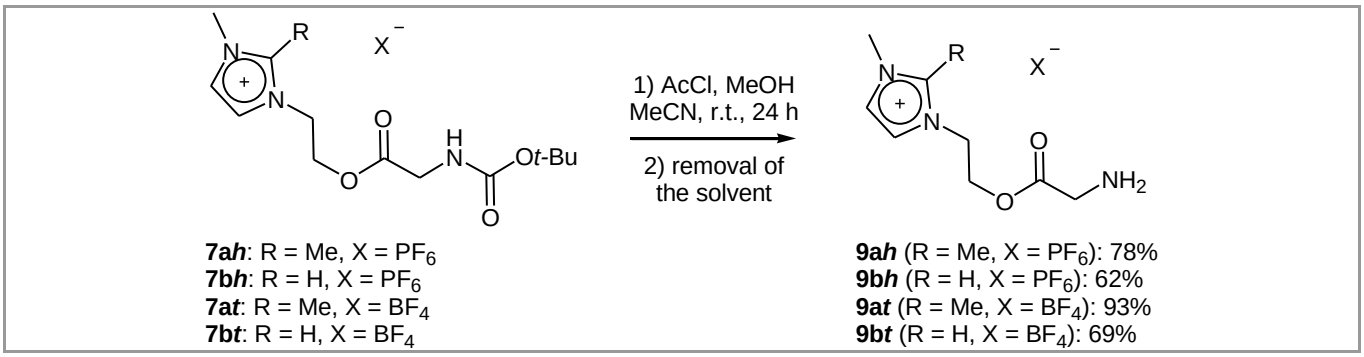

**Scheme 1**

NH-Boc and NH-formyl glycines were chosen to be grafted on the hydroxylated arm of synthesized ionic liquids. The esterification of the protected aminoacids **5**,**6** was effected with the ionic liquids **4c**,**d** in dry acetonitrile in the presence of dicyclohexylcarbodiimide (DCC) and a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine (DMAP), by adapting a procedure described.[4a] Dicyclohexylurea was easily removed by filtration, and washings of the crude residue with ethyl acetate or diethyl ether were efficient to afford the pure expected imidazolium salts **7**,**8** in yields ranging from 74 to 96% (Scheme 2). On the other hand, the ionic liquid **4b*h*** proved to be a bad support due to its good solubility in ethyl acetate or diethyl ether, which does not allow washings.




**Scheme 2**

The cleavage of Boc-protected amines **7** was next investigated. The use of trifluoroacetic acid in dichloromethane is often efficient for this purpose, but can cause a partial ionic liquid anion exchange with trifluoroacetate. We thus preferred to use hydrochloric acid in an organic solvent.[6e] Surprisingly, by treating acetonitrile solutions of the carbamates **7** with excess hydrochloric acid in ethyl acetate,[11] the amines were straight away obtained after the evaporation of acetonitrile instead of the attempted hydrochlorides, avoiding a subsequent neutralisation step.[12] The optimisation of the reactions was next carried out in NMR tubes by successively treating solutions of the carbamates **7** in $CD_3CN$ with methanol (1 equiv) and acetyl chloride (1 equiv). The monitoring of the reaction at room temperature showed that there was no more change after 24 h, and that the expected hydrochlorides were formed in about 50% conversion rates. Adding a second equiv of methanol and acetyl chloride to the NMR tubes led to the hydrochlorides in 100% conversions. Removal of the solvent from the reaction mixtures, washings and drying afforded the corresponding amines **9**, as verified by mass spectrometry, in good yields (Scheme 3).




**7a*h***: R = Me, X = $PF_6$
**7b*h***: R = H, X = $PF_6$
**7a*t***: R = Me, X = $BF_4$
**7b*t***: R = H, X = $BF_4$

**9a*h*** (R = Me, X = $PF_6$): 78%
**9b*h*** (R = H, X = $PF_6$): 62%
**9a*t*** (R = Me, X = $BF_4$): 93%
**9b*t*** (R = H, X = $BF_4$): 69%

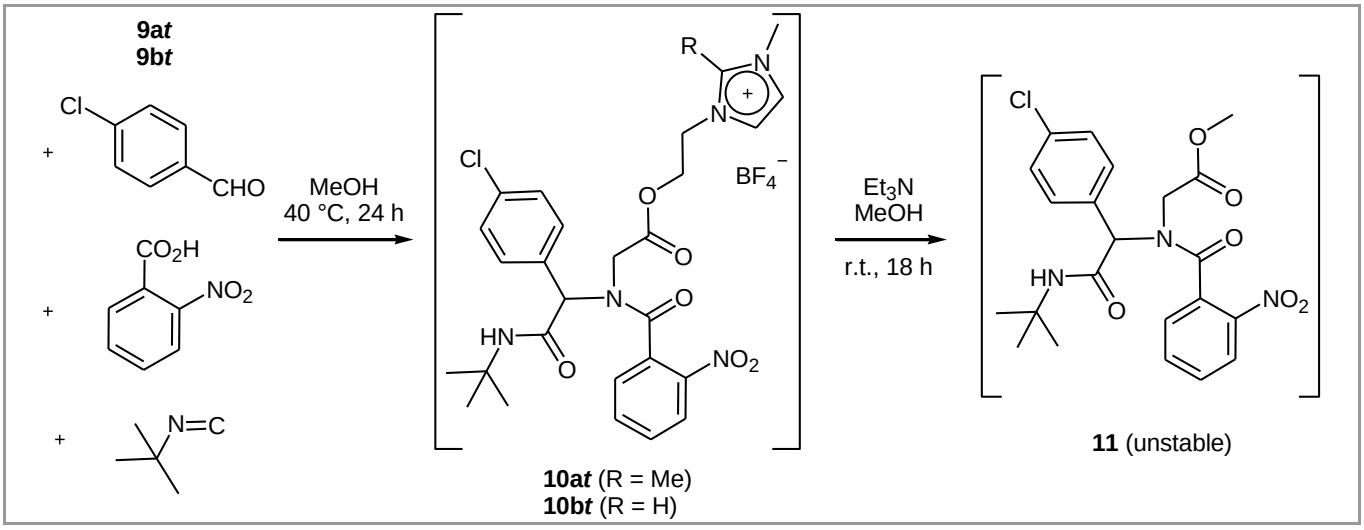
**Scheme 3**

Since the Boc cleavage was found to work satisfactorily, we did not study the formyl cleavage of **8**. We rather decided to involve the amines **9** in a multicomponent reaction utilizing isonitriles.

Among the multi-component transformations using amines, the Ugi four-component reaction (U-4CR) which involves amine, aldehyde, carboxylic acid and isonitrile, is one of the most frequently employed process.[13]

Preliminary studies in order to compare the different ionic supports were realized by treating the *O*-gratfed glycines **9** with 4-chlorobenzaldehyde, 2-nitrobenzoic acid and *tert*-butylisonitrile in methanol at room temperature or 40 °C.[14] Even if the Ugi compounds were partially cleaved from the ionic support during the reactions, it could be noted that the imidazolium ring (substituted at C2 or not) was compatible with *tert*-butylisonitrile under the conditions used.[15] Moreover, the Ugi reactions were found to be more efficient using the borate anion.

The subsequent treatment of partially cleaved Ugi compounds **10*t*** with triethylamine[16] in methanol at room temperature furnished the corresponding methyl ester **11**; the latter was identified by characteristic NMR peaks and mass spectrometry, but was insufficiently stable to be purified (Scheme 4).



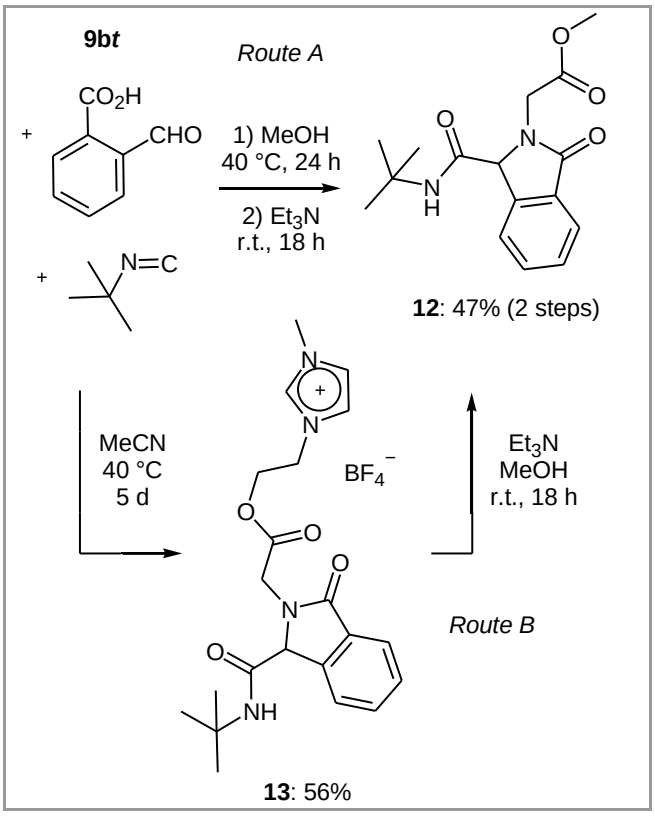

**10a*t*** (R = Me)
**10b*t*** (R = H)

**11** (unstable)

**Scheme 4**

On the other hand, the reaction between the amine **9b*t***, phthalaldehydic acid and *tert*-butylisonitrile,[17] followed by the cleavage from the ionic support, furnished a stable compound. Indeed, the ester **12** could be easily purified by chromatography over silica gel and crystallisation (Scheme 5, *Route A*).

In order to avoid partial cleavage during the Ugi reaction, we decided to use a solvent different from methanol. The Ugi reaction was performed in acetonitrile. The solubility of the amine **9b*t*** in acetonitrile is very low but using a long reaction time (5 days), we could obtain the *O*-grafted ester **13** in a 56% yield without observing cleavage or degradation. The unreacted amine **9b*t*** could be easily removed by filtration, giving after evaporation of acetonitrile and washings with diethyl ether the attempted Ugi product **13**. Subsequent cleavage under the conditions used before finally afforded the compound **12** in a 80% yield (Scheme 5, *Route B*).




**Scheme 5**

## Conclusion

We have shown that amines can be very easily prepared from the corresponding NH-Boc using ionic liquids as supports. This ionic liquid supported synthesis involving amines or derivatives offers the advantage of simple products isolations using washings with appropriate solvents; moreover, NMR monitorings of reactions proved to be easily feasible. The imidazolium-type ionic liquids *O*-bound glycine derivatives thus prepared can be used in Ugi reaction.

The $^{1}H$ and $^{13}C$ NMR spectra were recorded at 200 and 50 MHz, respectively, on a Bruker ARX 200 P spectrometer. *N*-Formylglycine (**6**) was prepared by adapting a procedure described.[18] The ionic liquids **3d**,[4b] **4dh**[10] and **4dt**[10] were prepared according to literature procedures.

### 2-Ethyl-1-methylimidazole (2a).[19]

To a biphasic mixture obtained from 2-ethylimidazole (**1a**, 9.8 g, 0.10 mol), tetrabutylammonium iodide (1.9 g, 5.1 mmol), 50% aqueous NaOH (350 mL) and toluene (280 mL), was added iodomethane (7.1 mL, 0.11 mol). After stirring for 15 min at r.t., the mixture was diluted with toluene (280 mL) and water (280 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under reduced pressure.

Pale yellow oil; yield: 9.8 g (89%).

IR (KBr): 3390, 2977, 2940, 1529, 1501, 1470, 1416, 1283,1146, 1059, 730, 623 $cm^{-1}$.

$^{1}H$ NMR ($CDCl_3$) δ = 6.90 (d, *J* = 1.1 Hz, 1 H), 6.77 (d, *J* = 1.1 Hz, 1 H), 3.55 (s, 3 H), 2.66 (q, *J* = 7.5 Hz, 2 H), 1.31 (t, *J* = 7.6 Hz, 3 H).

$^{13}C$ NMR ($CDCl_3$) δ = 147.5, 124.8, 118.7, 30.5, 18.2, 10.1.

Anal. Calcd for $C_6H_{10}N_2$ (110.16): C, 65.42; H, 9.15; N, 25.43. Found: C, 65.31; H, 9.32; N, 25.21.

### 1-Methyl-2-phenylimidazole (2b).

To a biphasic mixture obtained from 2-phenylimidazole (**1b**, 10 g, 69 mmol), tetrabutylammonium iodide (1.9 g, 5.1 mmol), 50% aqueous NaOH (350 mL) and toluene (280 mL), was added iodomethane (4.9 mL, 76 mmol). After stirring for 15 min at r.t., the mixture was diluted with toluene (280 mL) and water (280 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under reduced pressure.

Pale yellow oil; yield: 11 g (97%).

Anal. Calcd for $C_{10}H_{10}N_2$ (158.20): C, 75.92; H, 6.37; N, 17.71. Found: C, 75.68; H, 6.52; N, 17.44.

The spectroscopic data were identical to those previously described.[20]

**2-Ethyl-1-(2-hydroxyethyl)-3-methylimidazolium chloride (3a).**

A mixture of 2-chloroethanol (0.67 mL, 10 mmol) and 2-ethyl-1-methylimidazole (**2a**, 1.1 g, 10 mmol) was heated for 24 h at 120 °C. The crude product, which crystallized upon cooling, was finely crushed, washed with diethyl ether (3 x 80 mL), and dried under reduced pressure for 10 h.

Pale yellow powder; mp 55-58 °C; yield: 1.8 g (94%).

$^1$H NMR (DMSO-$d_6$) δ = 7.66 (s, 2 H), 6.79 (d, *J* = 1.1 Hz, 1 H), 5.25 (br s, 1 H), 4.20 (t, *J* = 4.9 Hz, 2 H), 3.82 (s, 3 H), 3.71 (t, *J* = 7,7 Hz, 2 H), 3.06 (q, *J* = 7,6 Hz, 2 H), 1.19 (t, *J* = 7,6 Hz, 3 H).

$^{13}$C NMR (DMSO-$d_6$) δ = 148.2 (q), 122.6 (t), 121.3 (t), 59.6 (s), 50.1 (s), 34.6 (p), 16.1 (s), 11.0 (p).

HRMS: *m*/*z* $C^+$ calcd for $C_8H_{15}N_2O$: 155.1184; found: 155.1176.

**1-(2-Hydroxyethyl)-2,3-dimethylimidazolium chloride (3b).**

The procedure is as described for **3a** but using 1-methyl-2-phenylimidazole (**2b**, 1.6 g, 10 mmol) instead of **2a**. Compound **3b** being too viscous to consider its washing, it was involved in the next step without purification.

**1-(2-Hydroxyethyl)-2,3-dimethylimidazolium chloride (3c).**

The procedure is as described for **3a** but using 1,2-dimethylimidazole (0.96 g, 10 mmol) instead of **2a**.

Beige powder; mp 58°C; yield: 1.6 g (88%).

$^1$H NMR (DMSO-$d_6$) δ = 7.59 (s, 2 H), 5.08 (t, *J* = 5.1 Hz, 1 H), 4.17 (t, *J* = 5.0 Hz, 2 H), 3.75 (s, 3 H), 3.68 (q, *J* = 4.8 Hz, 2 H), 2.57 (s, 3 H).

$^{13}$C NMR (DMSO-$d_6$) δ = 144.9, 122.2, 121.3, 59.7, 50.3, 34.8, 9.8.

HRMS: *m*/*z* $C^+$ calcd for $C_7H_{13}N_2O$: 141.10279; found: 141.1030.

**2-Ethyl-1-(2-hydroxyethyl)-3-methylimidazolium hexafluorophosphate (4a*h*).**

A mixture of **3a** (11 g, 56 mmol) and potassium hexafluorophosphate (10 g, 56 mmol) in MeCN (370 mL) was stirred for 24 h at r.t. in a dry atmosphere. After filtration over celite, removal of the solvent, and drying under reduced pressure, the product was kept under $N_2$.

Pale yellow powder; mp < 50 °C; yield: 17 g (99%).

$^1$H NMR (acetone-$d_6$) δ = 7.64 (d, *J* = 2.1 Hz, 1 H), 7.60 (d, *J* = 2.1 Hz, 1 H), 4.41 (t, *J* = 4.9 Hz, 2 H), 4.00 (s, 3 H), 3.96 (t, *J* = 5.0 Hz, 2 H), 3.24 (q, *J* = 7.7 Hz, 2 H), 1.37 (t, *J* = 7.7 Hz, 3 H), OH not seen.

$^{13}$C NMR (DMSO-$d_6$) δ = 148.2, 122.6, 121.3, 59.6, 50.1, 34.6, 16.2, 11.0.

HRMS: *m*/*z* $[2C^+, PF_6^-]^+$ calcd for $C_{16}H_{30}N_4O_2F_6P$: 455.2011; found: 455.2011.

**1-(2-Hydroxyethyl)-3-methyl-2-phenylimidazolium hexafluorophosphate (4b*h*).**

The procedure is as described for **4a*h*** but using **3b** (13 g, 56 mmol) instead of **3a**.

Beige powder; mp < 50 °C; yield: 17 g (88%).

$^1$H NMR (acetone-$d_6$) δ = 7.91 (d, *J* = 2.0 Hz, 1 H), 7.8 (m, 6 H), 4.26 (t, *J* = 5.0 Hz, 2 H), 3.92 (t, *J* = 5.1 Hz, 2 H), 3.87 (s, 3 H), OH not seen.

$^{13}$C NMR (DMSO-$d_6$) δ = 144.8, 132.4, 130.9, 129.6, 123.5, 122.1, 121.5, 59.4, 50.9, 35.6.

HRMS: *m*/*z* $C^+$ calcd for $C_{12}H_{15}N_2O$: 203.11844; found: 203.1184.

**1-(2-Hydroxyethyl)-2,3-dimethylimidazolium hexafluorophosphate (4c*h*).**

The procedure is as described for **4a*h*** but using **3c** (9.9 g, 56 mmol) instead of **3a**.

Pale brown oil; yield: 16 g (98%).

$^1$H NMR (acetone-$d_6$) δ = 7.60 (s, 1 H), 7.58 (s, 1 H), 4.39 (t, *J* = 4.6 Hz, 2 H), 3.97 (m, 6 H), 2.77 (s, 3 H).

$^{13}$C NMR (acetone-$d_6$) δ = 145.9, 122.8, 121.8, 60.9, 51.1, 35.0, 9.4.

HRMS: *m*/*z* $[2C^+, PF_6^-]^+$ calcd for $C_{14}H_{26}N_4O_2F_6P$: 427.16976; found: 427.1700.

**1-(2-Hydroxyethyl)-2,3-dimethylimidazolium tetrafluoroborate (4c*t*).**

A mixture of **3c** (11 g, 56 mmol) and ammonium tetrafluoroborate (5.9 g, 56 mmol) in MeCN (370 mL) was stirred for 24 h at r.t. in a dry atmosphere. After filtration over celite, removal of the solvent, and drying under reduced pressure, the product was kept under $N_2$.

Pale brown oil; yield: 13 g (99%).

$^1$H NMR (DMSO-$d_6$) δ = 7.63 (s, 2 H), 5.25 (t, *J* = 5.5 Hz, 1 H), 4.19 (t, *J* = 5.0 Hz, 2 H), 3.76 (s, 3 H), 3.67 (q, *J* = 4.8 Hz, 2 H), 2.59 (s, 3 H).

$^{13}$C NMR (acetone-$d_6$) δ = 145.9, 122.7, 121.8, 60.9, 51.0, 35.0, 9.4.

HRMS: *m*/*z* $[2C^+, BF_4^-]^+$ calcd for $C_{14}H_{26}N_4O_2F_4{}^{11}B$: 369.20849; found: 369.2091.

**1-[2-[(*N*-(*tert*-butoxycarbonyl)aminomethyl)carbonyloxy]ethyl]-**

**2,3-dimethylimidazolium hexafluorophosphate (7a*h*).**

1,3-Dicyclohexylcarbodiimide (0.89 g, 4.3 mmol) and 4-(dimethylamino)pyridine (26 mg, 0.21 mmol) were added to a solution of **4c*h*** (1.2 g, 4.3 mmol) in MeCN (30 mL) at r.t. After 10 min, *N*-(*tert*-butoxycarbonyl)glycine (**5**, 0.79 g, 4.5 mmol) was introduced, and the mixture was stirred for 24 h at r.t. before filtration over celite, removal of the solvent, washing with diethyl ether (2 x 80 mL) and 1:1 AcOEt/pentane (80 mL), and drying under reduced pressure for 10 h.

Beige powder; mp 120 °C; yield: 1.8 g (96%).

$^1$H NMR (acetone-$d_6$) δ = 7.71 (d, *J* = 2.2 Hz, 1 H), 7.64 (d, *J* = 2.1 Hz, 1 H), 6.40 (br s, 1 H), 4.67 (t, *J* = 4.6 Hz, 2 H), 4.55 (t, *J* = 4.5 Hz, 2 H), 3.98 (s, 3 H), 3.82 (d, *J* = 6.2 Hz, 2 H), 2.85 (s, 3 H), 1.40 (s, 9 H).

$^{13}$C NMR (acetone-$d_6$) δ = 170.8, 156.9, 146.5, 123.5, 122.3, 79.5, 63.4, 48.0, 42.7, 35.6, 28.5, 10.0.

HRMS: *m*/*z* $C^+$ calcd for $C_{14}H_{24}N_3O_4$: 298.17668; found: 298.1764.

**1-[2-[(*N*-(*tert*-butoxycarbonyl)aminomethyl)carbonyloxy]ethyl]-3-methylimidazolium hexafluorophosphate (7b*h*).**

The procedure is as described for **7a*h*** but using **4d*h*** (1.2 g, 4.3 mmol) instead of **4c*h***.

White powder; mp 70 °C; yield: 1.7 g (92%).

$^1$H NMR (acetone-$d_6$) δ = 9.13 (s, 1 H), 7.85 (s, 1 H), 7.76 (s, 1 H), 6.46 (br s, 1 H), 4.70 (t, *J* = 4.7 Hz, 2 H), 4.61 (t, *J* = 4.7 Hz, 2 H), 4.11 (s, 3 H), 3.86 (d, *J* = 6.2 Hz, 2 H), 1.41 (s, 9 H).

$^{13}$C NMR (acetone-$d_6$) δ = 170.8, 157.0, 138.0, 124.7, 123.8, 79.5, 63.2, 49.5, 42.7, 36.7, 28.5.

HRMS: *m*/*z* [$2C^+$, $PF_6^-$]$^+$ calcd for $C_{26}H_{44}N_6O_8F_6P$: 713.28625; found: 713.2862.

**1-[2-[(*N*-(*tert*-butoxycarbonyl)aminomethyl)carbonyloxy]ethyl]-2,3-dimethylimidazolium tetrafluoroborate (7a*t*).**

The procedure is as described for **7a*h*** but using **4c*t*** (0.98 g, 4.3 mmol) instead of **4c*h***.

White powder; mp 128 °C; yield: 1.5 g (90%).

$^1$H NMR (acetone-$d_6$) δ = 7.68 (d, *J* = 2.0 Hz, 1 H), 7.63 (d, *J* = 1.9 Hz, 1 H), 6.36 (br s, 1 H), 4.63 (t, *J* = 4.5 Hz, 2 H), 4.55 (t, *J* = 4.5 Hz, 2 H), 3.95 (s, 3 H), 3.81 (d, *J* = 6.2 Hz, 2 H), 2.82 (s, 3 H), 1.41 (s, 9 H).

$^{13}$C NMR (acetone-$d_6$) δ = 170.8, 156.9, 146.5, 123.5, 122.2, 79.4, 63.5, 47.9, 42.7, 35.5, 28.5, 9.8.

HRMS: *m*/*z* $C^+$ calcd for $C_{14}H_{24}N_3O_4$: 298.17668; found: 298.1771.

**1-[2-[(*N*-(*tert*-butoxycarbonyl)aminomethyl)carbonyloxy]ethyl]-3-methylimidazolium tetrafluoroborate (7b*t*).**

The procedure is as described for **7a*h*** but using **4d*t*** (0.92 g, 4.3 mmol) instead of **4c*h***.

White powder; mp 95 °C; yield: 1.5 g (92%).

$^1$H NMR (acetone-$d_6$) δ = 9.10 (s, 1 H), 7.83 (s, 1 H), 7.74 (s, 1 H), 6.41 (br s, 1 H), 4.67 (t, *J* = 4.7 Hz, 2 H), 4.59 (t, *J* = 4.7 Hz, 2 H), 4.08 (s, 3 H), 3.85 (d, *J* = 6.2 Hz, 2 H), 1.40 (s, 9 H).

$^{13}$C NMR (acetone-$d_6$) δ = 170.9, 156.9, 138.2, 124.7, 123.8, 79.4, 63.3, 49.5, 43.8, 36.6, 28.5.

HRMS: *m*/*z* $C^+$ calcd for $C_{13}H_{22}N_3O_4$: 284.16103; found: 284.1613.

**1-[2-[(Formylaminomethyl)carbonyloxy]ethyl]-2,3-dimethylimidazolium hexafluorophosphate (8a*h*).**

The procedure is as described for **7a*h*** but using *N*-formylglycine (**6**, 0.46 g, 4.5 mmol) instead of **5**, and washing with AcOEt (3 x 50 mL).

Beige powder; mp 116 °C; yield: 1.2 g (74%).

$^1$H NMR (DMSO-$d_6$) δ = 8.45 (br s, 1 H), 8.08 (s, 1 H), 7.64 (s, 1 H) 7.63 (s, 1 H), 4.40 (s, 4 H), 3.86 (d, *J* = 6.2 Hz, 2 H), 3.75 (s, 3 H), 2.60 (s, 3 H).

$^{13}$C NMR (DMSO-$d_6$) δ = 169.3, 161.9, 145.2, 122.5, 121.3, 62.8, 46.5, 39.4, 34.8, 9.3.

HRMS: *m*/*z* $C^+$ calcd for $C_{10}H_{16}N_3O_3$: 226.11917; found: 226.1188.

**1-[2-[(Formylaminomethyl)carbonyloxy]ethyl]-3-methylimidazolium hexafluorophosphate (8b*h*).**

The procedure is as described for **7a*h*** but using **4d*h*** (1.2 g, 4.3 mmol) instead of **4c*h***, *N*-formylglycine (**6**, 0.46 g, 4.5 mmol) instead of **5**, and washing with AcOEt (3 x 50 mL).

Pale brown oil; yield: 1.2 g (76%).

$^1$H NMR (acetone-$d_6$) δ = 9.06 (s, 1 H), 8.21 (s, 1 H), 7.81 (s, 1 H), 7.70 (s, 1 H), 7.64 (br s, 1 H), 4.70 (t, *J* = 4.4 Hz, 2 H), 4.58 (t, *J* = 4.5 Hz, 2 H), 4.07 (s, 3 H), 4.02 (d, *J* = 6.1 Hz, 2 H).

$^{13}$C NMR (acetone-$d_6$) δ = 170.0, 162.7, 138.0, 124.7, 123.7, 63.5, 49.4, 40.3, 36.6.

HRMS: *m*/*z* $C^+$ calcd for $C_9H_{14}N_3O_3$: 212.1035; found: 212.1036.

**1-[2-[(Formylaminomethyl)carbonyloxy]ethyl]-2,3-dimethylimidazolium tetrafluoroborate (8a*t*).**

The procedure is as described for **7a*h*** but using **4c*t*** (0.98 g, 4.3 mmol) instead of **4c*h***, *N*-formylglycine (**6**, 0.46 g, 4.5 mmol) instead of **5**, and washing with AcOEt (3 x 50 mL).

White powder; mp 54 °C; yield: 1.1 g (80%).

$^1$H NMR (DMSO-$d_6$) δ = 8.44 (br s, 1 H), 8.08 (s, 1 H), 7.64 (s, 1 H) 7.63 (s, 1 H), 4.41 (s, 4 H), 3.86 (d, *J* = 6.0 Hz, 2 H), 3.75 (s, 3 H), 2.63 (s, 3 H).

$^{13}$C NMR (DMSO-$d_6$) δ = 169.3, 161.9, 145.1, 122.5, 121.3, 62.8, 46.6, 39.4, 34.8, 9.3.

HRMS: *m*/*z* $C^+$ calcd for $C_{10}H_{16}N_3O_3$: 226.1192; found: 226.1188.

**1-[2-[(Formylaminomethyl)carbonyloxy]ethyl]-3-methylimidazolium tetrafluoroborate (8b*t*).**

The procedure is as described for **7a*h*** but using **4d*t*** (0.92 g, 4.3 mmol) instead of **4c*h***, *N*-formylglycine (**6**, 0.46 g, 4.5 mmol) instead of **5**, and washing with AcOEt (3 x 50 mL).

Pale brown oil; yield: 1.2 g (96%).

$^1$H NMR (acetone-$d_6$) δ = 9.04 (s, 1 H), 8.20 (s, 1 H), 7.81 (s, 1 H), 7.70 (s, 1 H), 7.61 (br s, 1 H), 4.65 (t, *J* = 4.6 Hz, 2 H), 4.55 (t, *J* = 4.4 Hz, 2 H), 4.05 (s, 3 H), 4.01 (d, *J* = 6.1 Hz, 2 H).

$^{13}$C NMR (acetone-$d_6$) δ = 170.0, 162.7, 140.1, 124.7, 123.7, 63.7, 49.3, 40.3, 36.6.

HRMS: *m*/*z* $C^+$ calcd for $C_9H_{14}N_3O_3$: 212.10352; found: 212.1040.

**1-[2-[(Aminomethyl)carbonyloxy]ethyl]-2,3-dimethylimidazolium hexafluorophosphate (9a*h*).**

A solution of **7a*h*** (1.1 g, 2.5 mmol) in acetonitrile (5 mL) was successively treated with methanol (0.20 mL, 5.0 mmol) and acetyl chloride (0.36 mL, 5.0 mmol). After 24 h at r.t., the solvent was removed under reduced pressure. The residue was washed with AcOEt (2 x 10 mL) and dried under reduced pressure for 10 h.

Beige powder; mp 130 °C; yield: 0.67 g (78%).

$^1$H NMR (DMSO-$d_6$) δ = 8.54 (br s, 2 H), 7.73 (d, *J* = 1.9 Hz, 1 H), 7.66 (d, *J* = 1.9 Hz, 1 H), 4.46 (s, 4 H), 3.79 (s, 2 H), 3.77 (s, 3 H), 2.61 (s, 3 H).

$^{13}$C NMR (DMSO-$d_6$) δ = 167.2, 145.2, 122.6, 121.4, 63.7, 46.5, 39.8, 34.9, 9.6.

HRMS: *m*/*z* $C^+$ calcd for $C_9H_{16}N_3O_2$: 198.12425; found: 198.1245.

**1-[2-[(Aminomethyl)carbonyloxy]ethyl]-3-methylimidazolium hexafluorophosphate (9b*h*).**

The procedure is as described for **9a*h*** but using **7b*h*** (1.1 g, 2.5 mmol) instead of **7a*h***.

Beige powder; mp 153 °C; yield: 0.51 g (62%).

$^1$H NMR (DMSO-$d_6$) δ = 9.24 (s, 1 H), 8.25 (br s, 2 H), 7.81 (s, 1 H), 7.73 (s, 1 H), 4.49 (s, 4 H), 3.87 (s, 3 H), 3.80 (s, 2 H).

$^{13}$C NMR (acetone-$d_6$) δ = 167.0, 137.3, 123.5, 122.6, 63.5, 47.8, 39.6, 35.8.

HRMS: *m*/*z* $C^+$ calcd for $C_8H_{14}N_3O_2$: 184.10860; found: 184.1087.

**1-[2-[(Aminomethyl)carbonyloxy]ethyl]-2,3-dimethylimidazolium tetrafluoroborate (9a*t*).**

The procedure is as described for **9a*h*** but using **7a*t*** (0.96 g, 2.5 mmol) instead of **7a*h***.

White powder; mp 159 °C; yield: 0.66 g (93%).

$^1$H NMR (DMSO-$d_6$) δ = 8.44 (br s, 2 H), 7.73 (s, 1 H), 7.65 (s, 1 H), 4.46 (s, 4 H), 3.79 (s, 2 H), 3.76 (s, 3 H), 2.61 (s, 3 H).

$^{13}$C NMR (DMSO-$d_6$) δ = 167.3, 145.2, 122.5, 121.4, 63.7, 46.4, 39.8, 34.9, 9.6.

HRMS: *m*/*z* $C^+$ calcd for $C_9H_{16}N_3O_2$: 198.1243; found: 198.1245.

**1-[2-[(Aminomethyl)carbonyloxy]ethyl]-3-methylimidazolium tetrafluoroborate (9b*t*).**

The procedure is as described for **9a*h*** but using **7b*t*** (0.93 g, 2.5 mmol) instead of **7a*h***.

White powder; mp 125-126 °C; yield: 0.47 g (69%).

$^1$H NMR (DMSO-$d_6$) δ = 9.26 (s, 1 H), 8.41 (br s, 2 H), 7.82 (s, 1 H), 7.73 (s, 1 H), 4.50 (s, 4 H), 3.87 (s, 3 H), 3.82 (s, 2 H).

$^{13}$C NMR (DMSO-$d_6$) δ = 167.1, 137.4, 123.6, 122.7, 63.6, 47.9, 39.7, 35.9.

HRMS: *m*/*z* $C^+$ calcd for $C_8H_{14}N_3O_2$: 184.10860; found: 184.1087.

**1-[2-[[*N*-[1-(4-chlorophenyl)-2-[(1,1-dimethylethyl)amino]-2-oxoethyl]-*N*-[(2-nitro-phenyl)carbonyl]aminomethyl]carbonyloxy]ethyl]-2,3-dimethylimidazolium tetrafluoroborate (10a*t*).**

4-Chlorobenzaldehyde (0.16 g, 1.1 mmol) was added to a solution of **9a*t*** (0.29 g, 1.0 mmol) in methanol (2 mL). After 10 min at 40°C, 2-nitrobenzoic acid (0.19 g, 1.1 mmol) and *tert*-butylisonitrile (127 μL, 1.1 mmol) were added to the mixture in a dry atmosphere. After 24 h at 40 °C, the solvent was removed under reduced pressure, the residue was washed with diethyl ether (2 x 10 mL) and dissolved in acetonitrile (4 mL). After filtration and evaporation of the filtrate, the residue was dried under reduced pressure for 10 h.

HRMS: *m*/*z* $C^+$ calcd for $C_{28}H_{33}N_5O_6{}^{35}Cl$: 570.21194; found: 570.2117.

**1-[2-[[*N*-[1-(4-chlorophenyl)-2-[(1,1-dimethylethyl)amino]-2-oxoethyl]-*N*-[(2-nitro-phenyl)carbonyl]aminomethyl]carbonyloxy]ethyl]-3-methylimidazolium tetrafluoroborate (10b*t*).**

The procedure is as described for **10a*t*** but using **9b*t*** (0.27 g, 1.0 mmol) instead of **9a*t***.

HRMS: *m*/*z* $C^+$ calcd for $C_{27}H_{31}N_5O_6{}^{35}Cl$: 556.19629; found: 556.1968.

### 1-[2-[[*N*-[3-(*tert*-butylaminocarbonyl)] phthalimidino]carbonyloxy]ethyl]-3-methylimidazolium tetrafluoroborate (13).

Phthalaldehydic acid (0.17 g, 1.1 mmol) was added to a solution of **9b*t*** (0.27 g, 1.0 mmol) in MeCN (4 mL). After 20 min at 40°C, *tert*-butylisonitrile (127 µL, 1.1 mmol) was added to the mixture. After 5 d at 40 °C, the mixture was filtered in order to remove the unreacted amine. The solvent was then removed under reduced pressure, and the residue was washed with diethyl ether (2 x 10 mL) and dried under reduced pressure for 10 h.

Pale brown oil; yield: 0.27 g (56%).

$^1$H NMR (acetone-$d_6$) δ = 9.04 (s, 1 H), 8.08 (s, 1 H), 8.07 (s, 1 H), 7.7 (m, 4 H), 6.72 (s, 1 H), 5.29 (s, 1 H), 4.6 (m, 3 H), 4.0 (m, 6 H), 1.31 (s, 9 H).

$^{13}$C NMR (acetone-$d_6$) δ = 169.3, 168.5, 166.4, 142.9, 137.6, 134.9, 131.3, 131.2, 125.1, 124.2, 124.0, 123.1, 65.1, 63.4, 51.5, 48.7, 43.5, 36.0, 26.9 (3C).

HRMS: *m*/*z* $C^+$ calcd for $C_{21}H_{27}N_4O_4$: 399.2032; found: 399.2033.

### Methyl [*N*-[3-(*tert*-butylaminocarbonyl)] phthalimidino]acetate (12).

***Route A.***

Phthalaldehydic acid (0.17 g, 1.1 mmol) was added to a solution of **9b*t*** (0.27 g, 1.0 mmol) in methanol (2 mL). After 20 min at 40°C, *tert*-butylisonitrile (127 µL, 1.1 mmol) was added to the mixture in a dry atmosphere. After 24 h at 40 °C, the mixture was cooled to r.t. and triethylamine (0.21 µL, 1.5 mmol) was added. After stirring for 18 h at r.t., removal of the solvent, addition of water (5 mL), extraction with AcOEt, drying over $MgSO_4$, and evaporation of the solvent, the crude product was chromatographed over silica gel using AcOEt/pentane (1/1) as an eluent and crystallized from diethyl ether.

***Route B.***

A solution of **13** (0.49 g, 1 mmol) in methanol (3 mL) was treated with triethylamine (0.21 µL, 1.5 mmol), and stirred for 18 h at r.t. in a dry atmosphere. After removal of the solvent, addition of water (5 mL), extraction with AcOEt, drying over $MgSO_4$, and evaporation of the solvent, the crude product was chromatographed over silica gel using AcOEt/pentane (1/1) as an eluent.

Beige powder; mp 148-150 °C; yield: 0.14 g (47%, 2 steps) using route A and 0.24 g (80%) using route B.

$^1$H NMR (acetone-$d_6$) δ = 7.7 (m, 5 H), 5.22 (s, 1 H), 4.68 (d, *J* = 18 Hz, 1 H), 4.01 (d, *J* = 18 Hz, 1 H), 3.74 (s, 3 H), 1.31 (s, 9 H).

$^{13}$C NMR (acetone-$d_6$) δ = 170.7, 169.6, 166.8, 143.2, 132.9, 131.6, 129.4, 123.3, 104.0, 65.7, 52.5, 51.9, 43.7, 28.3 (3C).

Anal. Calcd for $C_{16}H_{20}N_2O_4$ (304.14): C, 63.14; H, 6.62; N, 9.20. Found: C, 63.29; H, 6.64; N, 9.08.

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